PROTECTING HUMAN SUBJECTS

Office of Biological and Environmental Research • U.S. Department of Energy • Winter 1999/2000

This issue of the newsletter* Protecting Human Subjects *concentrates on discussions held during DOE's meeting, "Workers as Research Subjects: A Vulnerable Population?" The meeting was held in Bethesda, Maryland, June 24–25, 1999.

Workers: *Vulnerable as research subjects*

The following are synopses of talks presented at the DOE meeting, "Workers as Research Subjects: A Vulnerable Population?"

DOE Human Subjects Program Manager Susan Rose organized and chaired the meeting, which focused on issues that arise when the work force (federal, military, or industry) becomes the subject of research.

The conference achieved its primary goal—raising awareness of the seriousness and complexity of issues related to workers as subjects, including their vulnerability to potential coercion or exposure to risk.

An educational process

The purpose of the meeting was educational in nature and was not meant to arrive at consensus regarding workers as a vulnerable population but rather to explore the evolving issues and perspectives for workers as human subjects in research studies.

The intention was that attendees would take back to their own organizations the ideas and concepts expressed during the conference. Such an educational process may enlighten and influence others who lacked knowledge of the subject matter or have held misguided views about workers and the research environment. Several innovative models were presented for addressing workers in research in a variety of situations.

The conference also provided an exceptional opportunity for stakeholders (workers, researchers, unions, industry, and military) to openly express themselves. Extensive networking and informal exchange of ideas and experiences among the participants was encouraged.

No substantive conclusions can be drawn from the meeting except perhaps that speakers agreed that any study should be considered "research" if it uses workers to gain generalizable knowledge. Perhaps this position will now be developed in a way that will provide greater protection of workers in research environments.

Reports from the talks are divided into five sections, reflecting the five sessions of the meeting.

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Inside

SESSION 1
Setting the stage

Speaker: Paul Brandt-Rauf, Columbia University.

Topic: *ABCs of Workplace Health Research.*
It has been suggested that workers may be the "miner's canary" for the rest of society. On an ordinary day in some workplaces, they may be exposed to potentially toxic substances. Only when adverse reactions are noted does society initiate a formal investigation of the substance's toxicity.

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In this way, workers may appear to be "experimental subjects" testing chemicals previously untried on humans. This is analogous to biomedical research but without the usual independent review that balances risks and benefits to the "research subjects" and ensures informed and voluntary prior consent by the "research subjects."

Counterarguments suggest that the economic structure of employment already addresses the risk/benefit and consent considerations. Society compensates hazardous work with "hazard pay," directly increasing the benefits to those who assume the risk. Furthermore, to the extent that risks are known, right-to-know mechanisms provide the worker with the information necessary for an informed consent.

Thus, armed with the knowledge of the benefits to be expected and the risks assumed, the worker may "volunteer" to take the risk or not. However, "voluntariness" requires more than information and the ability to articulate the word "no." It also requires freedom from coercion and undue influence. Indeed, a biomedical research Institutional Review Board (IRB) would view a study in which subjects received significant financial compensation—"hazard pay" as it were—with a sceptical eye. The concern would be that powerful incentives minimize the possibility for truly free consent.

Therefore, it seems doubtful that many workplace situations would satisfy the close scrutiny required of an IRB. Since our society has apparently decided that those fostering our biomedical progress as human research subjects deserve a high level of ethical scrutiny and protection, serious consideration should be given before denying this level of protection to those who foster our economic progress: the workers.

Speaker: Marjorie Speers, Deputy Associate Director for Centers for Disease Control and Prevention, Atlanta, Georgia.

Topic: *When Is It Research?*
Information is gathered for many purposes. Sometimes, it is to generate new, or contribute to current, knowledge; other times it is gathered to benefit individuals who provide the information, to set policy, or to improve programs.

In all cases, for information to be useful, it must be collected systematically, employing methods that reduce bias and increase utilization of the data. For this reason, it is often difficult to define a data collection activity as either research or nonresearch.

Yet, it is critical in our efforts to act ethically that scientists and practitioners accurately and consistently classify their data collection endeavors with respect to whether they are research. Research activities require that the individuals who participate in them be adequately protected from any potential harms.

Some surveillance projects, emergency responses, and program evaluations are research involving

Inspiration, support, commitment

A highlight of the "Workers as Research Subjects" meeting was the presentation of an award by Aristides Patrinos, Associate Director of the DOE Office of Biological and Environmental Research, to Susan Rose, Program Manager of DOE's Human Research Subjects Protection Program. The award was "in recognition of and appreciation for your continuing inspiration, support, and commitment to the protection of research subjects."

human subjects and others are not. Each project must be reviewed on a case-by-case basis. Although general guidance can be given to assist in classifying these activities as either research or nonresearch, no one criterion can be universally applied.

The decision regarding classification lies in the intent of the project. If the primary intent is to generate generalizable knowledge, the project is research. If the primary intent is to prevent or control disease or injury, and no research is presently intended, the project is not research.

If the primary intent changes to generating generalizable knowledge, the project becomes research.

Speaker: Reed B. Durham
Lockheed Martin Energy Systems, Y-12 Plant, Oak Ridge, Tennessee.

Topic: *LPT Positive: Is Life on Hold?*
Over the past 30 years working as an analytical chemist, I have encountered a number of hazardous materials. Some caused allergic reactions immediately; others had no effects at all. Probably none has had the lasting effect that beryllium has had.

I worked with beryllium compounds for a number of years performing a variety of analyses, all using the appropriate safety measures recommended at the time. I have since tested positive two times on the lymphocite proliferation test (LPT), followed by further examinations including the infamous lung washing. Fortunately, these tests were negative, but the stigma of the positive LPTs remains.

For all practical purposes, the tests for chronic beryllium disease (CBD) might as well have been positive. My activities in and around beryllium have been severely curtailed. This includes the supervision of other chemists who may be required to work with beryllium. All because the LPT was positive, even though the more definitive tests for CBD were negative.

Any expertise and experience with beryllium materials that I have acquired over the past 30 years is lost to the lab because I cannot be in the area where beryllium is even suspected. If this information had been disclosed to me initially, I am not sure I would have agreed to take the first LPT. I certainly have not recommended taking it to anyone working with me.

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> —Reed Durham

> *Despite awareness of its health risks, beryllium continues to be used in numerous industries, and so beryllium-related diseases continue to occur.*
>
> —Lisa Maier

Speaker: Lisa Maier, National Jewish Medical and Research Center Denver, Colorado.

Topic: *Introduction to Beryllium Disease.*
Despite awareness of its health risks, beryllium continues to be used in numerous high technological applications, including the aerospace, electronics, nuclear weapons, telecommunications and beryllium mining and manufacturing industries. Efforts have been made to reduce exposure to beryllium in the workplace, yet beryllium-related diseases continue to occur.

The manifestations of beryllium-related health effects vary. Less common presentations include beryllium skin disease and cancer. More commonly, beryllium exposure results in beryllium sensitization (BeS) and chronic beryllium disease (CBD). Beryllium dust is inhaled and causes an immune response in blood and lung cells of susceptible individuals.

> *"About 10% of these individuals will eventually develop CBD."*

About 10% of these (BeS) individuals will eventually develop CBD. Unfortunately, there is no cure for CBD, and current treatment is aimed at controlling the disease.

The primary treatment for CBD includes the use of prednisone, which suppresses the immune system nonspecifically.

Efforts are required to reduce beryllium disease, primarily by reducing exposure in the workplace. This can be accomplished by reducing the number of workers exposed to beryllium, using effective industrial hygiene controls, and educating and updating workers on workplace practices to limit exposure.

It is also important to combine beryllium surveillance measures with ongoing industrial hygiene efforts to alter high-risk jobs and practices. Finally, ongoing research is needed to develop new diagnostic tests to allow early diagnosis of beryllium health effects.

Speaker: Glenn Bell
Lockheed Martin Energy Systems, Y-12 Plant, Oak Ridge, Tennessee.

Topic: *Living with Beryllium Disease.*
Since being diagnosed with CBD in 1993, I have dedicated a large amount of my personal time and resources to educate myself and others about the history, hazards, and heartbreaks of this orphan disease.

I have had to cancel social outings, family reunions and even grocery shopping because of breathing and fatigue problems. I have had two potential relationships deteriorate and disappear because the partner could not or would not cope with the frequent health problems and the potential of their worsening.

As many who have taken steroids know, there are many side effects, most of which diminish or disappear when the Prednisone is discontinued, until the next episode.

I am disappointed that I have a disease that was probably preventable. I am disappointed that the workers were not told of the true dangers, or that the Departments of Defense and Energy did not do more for the workers when the DOD cases of beryllium disease appeared in

their facilities in the late seventies and early eighties.

Several things would help me and other victims. Minimizing legal entanglements would lessen the stress for victims and their families. An informational video, with victim/family interviews has been stifled by attorneys on both sides because of fear it would hurt their legal positions.

Speaker: Donna Cragle, Center for Epidemiologic Studies, Oak Ridge Institute for Science and Education.

Topic: *CBD Research: Risks and Benefits.*
Most research involving human subjects can be found to involve both risks and benefits. The risks accrue to individuals who participate, while the benefits accrue to a much wider community, including participants, nonparticipants, and the scientific community.

The most difficult part of conducting this type of research is honesty, stakeholder buy-in, and communication.

Speaker: John Campbell,
Retired Nevada Test Site Worker, Las Vegas, Nevada.

Topic: *Why I Am A Study Subject.*
I became involved in the Nevada Test Site Workers Study to identify and monitor health conditions caused by my having been a uranium miner.

The driving factor for me was that I was witnessing a sudden epidemic of cancer-related deaths and sickness in a lot of our former workers, particularly the workers from 1958. I believe we should have been informed and given a choice about any dangerous exposures.

Responsibility lies with those who knew and failed to inform, educate, and protect workers' health and welfare.

Speaker: Ellen L. Gadbois
Congressional Fellow,
Senate Committee on Health, Education, Labor, and Pensions, Washington, DC.

Topic: *Genetic Discrimination in the Workplace.*
Numerous bills have been introduced in the 105th and 106th Congresses to prohibit genetic discrimination in health insurance and the workplace. The Americans with Disabilities Act (ADA) placed some limitations on when an employer can access genetic information about an employee or potential employee and how genetic information may be used by an employer.

However, a recent survey by the American Management Association showed that a significant percentage of employers make employment decisions on the basis of genetic information. This issue will become more significant as our understanding of the genetic basis for disease increases through the Human Genome Project.

SESSION 2
Stakeholder views

Speaker: Robert J. Pleasure,
Executive Director, The Center to Protect Workers Rights, Building and Construction Trades Department, AFL-CIO, Washington, DC.

Topic: *Union Perspectives on Workplace Studies.*
Providing workers a voice in the design and implementation of biomedical and other research initiatives is a role that unions in the construction industry take as a serious obligation.

The impact on workers as research subjects goes beyond the immediate

"Providing workers a voice in the design and implementation of biomedical and other research initiatives is a role that unions in the construction industry take as a serious obligation.
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> *The U.S. Army . . . formed a novel relationship with the Seventh Day Adventist Church community to ensure availability of the church's conscientious objectors as potential human volunteer subjects.*
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> —Arthur Anderson

health risk of a medical procedure. The impact includes potentially devastating economic and social effects when disclosure of information can result in loss of employment or reduced opportunities for employment, inability to obtain life or health insurance, or even exclusion from a career or trade.

Further, research records and notification practices may affect the ability of workers or their surviving family members to obtain workers compensation for injury, illness, or death related to their employment, and it may impact future civil actions related to worker's injuries or illnesses.

In the construction industry, unions carry an additional ethical burden because of confidential medical and insurance records maintained by jointly administered health and welfare funds, collectively bargained workers, compensation programs, or union-owned insurance providers.

These records often provide the primary source of data for research on the causes of occupational injury and disease in the construction industry.

Such research has the potential to improve the future working conditions and quality of life of all construction workers and to provide the basis for just compensation for those workers who have already been made ill because of their work. But, disclosure may well impact the very members for whom these programs provide valuable benefits.

All Institutional Review Boards (IRBs) reviewing research involving workers as subjects should include an appropriate level of worker voice in their deliberations, because societal benefits are not easily balanced against individual risks.

Scientists, physicians, and ethicists may not fully appreciate the potential risks or the practicality of proposed research procedures.

Speaker: Richard Lippin, Medical Director, Lyondell Chemical Company, New Square, Pennsylvania.

Topic: *Ethical Dilemmas in the Occupational Medicine/Research Setting.*
Several issues should be addressed by the research and research-funding communities to strengthen the commitment to human subjects generally and workers as subjects specifically.

For example, there is not enough industry and industry-sponsored human research when compared to the much more significant industry-sponsored animal research. In addition, there are severe methodological limitations in the dominant reductionistic (single agent-single outcome) research model.

It would be helpful to replace it with a bio-psycho-social model of occupational medical research with a strong neuroscience component, especially as it relates to chronic multifactorial diseases such as cancer.

Trust, inherent in the doctor-patient relationship, is a necessary component in human research. But it is very difficult to achieve in the corporate setting. This issue has become especially complicated in a world of electronic medical information. But if managed responsibly and ethically, these new information systems hold great promise for the future of industry-based or industry-sponsored human research.

Speaker: Arthur Anderson, U.S,. Army Medical Research Institute of Infectious Diseases, Ft. Detrick, Maryland.

Topic: *Ethical Contributions and Dilemmas of Project White Coat.*
Project White Coat was a Cold War era research program that involved human subjects in development and testing of vaccines and drugs against agents considered biological warfare threats.

In 1953, all branches of the military received the Wilson Memorandum, which incorporated the Nuremberg Code as guidance for ethical use of human subjects in nuclear, biological, and chemical warfare research. The U.S. Army Medical Unit at Fort Detrick, which was created around this time, formed a novel relationship with the Seventh Day Adventist (SDA) Church community to ensure availability of the church's conscientious objectors as potential human volunteer subjects.

This relationship with the SDA church also served to amplify the influence of the Nuremberg Code principles and ensured external accountability for the work that would follow. A benefit to the Army was that SDA conscientious objectors readily volunteered for noncombat duty at Fort Detrick as human volunteer subjects. The risk was that coercive elements might be involved in this relationship.

History will show that both parties, the SDA church and the Army, were rigorous in respecting the principles of the Nuremberg Code and the persons who put themselves at risk so that vital information and products could be obtained.

Speaker: Phil Pittman, MD, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Maryland.

Topic: *Long-Term Follow-Up of White Coat Volunteers and Workers Receiving Repeated Immunizations with Multiple Vaccines.*
We are investigating the long-term health of medical research volunteers who participated in the Department of Defense–sponsored medical research. Of special interest are those who received repeated immunization with multiple vaccines.

Two groups have participated in clinical research. A total of 2300 soldiers participated in Project White Coat. Of these, 1800 participated in one or more research studies. These studies included vaccines for anthrax, plague, RMSF, Q-fever, Tularemia, Rift Valley fever, etc.

This current study will assess the current health of these pioneers as we approach the 25th anniversary of the termination of this program. This study involves a detailed health history questionnaire. A total of 423 volunteers have responded as of May 1, 1999.

The objective of the second study is to determine whether individuals who received multiple vaccines as a condition of employment at a high containment biologic laboratory demonstrate any adverse health effects over the long term.

A total of 570 study and control volunteers have been enrolled in this case-control study. Most study subjects received 150–200 vaccinations and skin tests, and some received more than 300 such injections during their tenure at Fort Detrick.

Speaker: Benjamin Rivera, Consultant, Silver Spring, Maryland.

Topic: *Soldiers as Subjects: Project White Coat.*
Today you make choices about how you want to live. You live or die by those choices. As a soldier you give your life to your country, and your country will, if possible, not put you in harm's way.

In Project White Coat, your country and your church gave you an opportunity to choose how to die. It was your choice until the day that you were exposed to the virus. Are workers, soldiers, and donors really free to choose? Are workers as research subjects and soldiers used as frogs?

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A story is told that if you put a frog in a hot pot of water, he will jump out before he is burned. But if you put the frog in a cold pot of water and heat it up slowly, the frog will boil to death.

—Benjamin Rivera

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A story is told that if you put a frog in a hot pot of water, he will jump out before he is burned. But if you put the frog in a cold pot of water and heat it up slowly, the frog will boil to death.

To be free to choose—whether you are a worker, soldier, or a civilian—your total involvement in the experiment should be managed by an independent organization. The organization should be created by persons who have been through the process.

SESSION 3
Innovative models

Speaker: Joseph J. Hurrell Jr., National Institute for Occupational Safety and Health, Cincinnati, Ohio.

Topic: *Protecting Participants in Work Site Research.*
The Division of Surveillance, Hazard Evaluations, and Field Studies (DSHEFS) conducts a variety of epidemiological field research involving human subjects.

This research assesses the incidence and prevalence of acute and chronic disease in the working population and their offspring; evaluates possible associations between work-related exposures and disease; and determines the nature and extent of occupational exposure to physical, chemical, and biological agents.

Industry-wide studies, studies of workers at the Department of Energy and other energy-related facilities, as well as legislatively mandated and narrowly focused work site health hazard evaluations are conducted by DSHEFS investigators. These studies involve a variety of human subject protection issues that were discussed in this presentation.

Speaker: Mitchell Singal, National Institute for Occupational Safety and Health, Cincinnati, Ohio.

Topic: *The NIOSH Health Hazard Evaluation Program.*
The National Institute for Occupational Safety and Health (NIOSH) conducts occupational health hazard evaluations (HHEs) at the request of employers, unions, or employees.

Many of these HHEs are solely environmental investigations, but others involve medical evaluations. Although most of the latter HHEs are clinical (that is, public health) investigations, which do not require review by the NIOSH Human Subjects Review Board (HSRB), informed consent is obtained and participants are notified of their medical test results, just as in HSRB-approved studies.

A minority of proposed HHE-based studies meets the criteria for human subjects research and must have HSRB approval before being carried out. For some other HHEs, HSRB review is requested for various reasons, even though it may not actually be required.

Speaker: Michael J. Colligan, National Institute for Occupational Safety and Health, Cincinnati, Ohio.

Topic: *NIOSH IRB Practices for Work Site Research.*
Workplace research presents unique challenges to Institutional Review Boards that are responsible for protecting the rights and welfare of employees as study participants.

Special considerations arise because the workplace is a "closed community" in which members of the organization have established enduring relationships that exist independently of the life of the study.

Individuals know one another, interact on a daily basis, and are collectively (though not always similarly) impacted by the results of the research. Consequently, a worker's right to decide whether to participate in a study may be compromised by real or imagined pressures from supervisors and coworkers. This not only diminishes the voluntary quality of the consent process but may also fractionalize the work force into "study supporters" and "study resisters."

Researchers need to make sure that recruiting and consent procedures are structured in such a way as to minimize conformity pressures and stress the voluntary nature of participation. Other problems arise in drawing a distinction between research and nonresearch activities.

An organization, for example, may have a mandatory health monitoring program in which workers are required to undergo periodic physical examinations and biomedical testing. The purpose is to detect the early signs of health problems so that remedial steps can be taken.

Participation in the program is not voluntary, but rather is a condition of employment. Such programs are not typically considered research and do not require review and approval by an IRB. Using these same data for more general hypothesis testing about the relationship between antecedent events (e.g., workplace exposures) and nonclinical outcomes (e.g., biomarker status) does constitute research, however, and would require IRB review.

It is important that both data gatherers (researchers) and data providers (participants) have a clear understanding of the distinction between research and routine programmatic activities so that the necessary review and consent procedures can take place. Finally, because of the "closed community" nature of the workplace, researchers must make a special effort to protect the confidentiality of worker data. The collection and integration of sensitive information on workers raises the risk that other members within the organization (e.g., coworkers, supervisors, managers) may gain access to it.

Even records which have been stripped of such personal identifiers as names, social security numbers, or payroll numbers may be linkable to individual workers based on demographic profiles (e.g., length of service, department, gender, and age) recognizable by others within the organization. Careful attention must be paid to the data collection and management procedures to protect those who have volunteered to participate.

SESSION 4
Myth of privacy?

Speaker: Yvonne Sherman,
U.S. Department of Energy,
Richland, Washington.

Topic: *The Privacy Act Protects Whom?*
This presentation included a discussion of the Privacy Act and its impact on worker health studies involving federally owned records.

The situation: The Privacy Act of 1974 requires that the federal government protect personal information located in government-owned records from unauthorized disclosures. It requires that the government withhold personal information

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from everyone but the subject of the information—with certain specific exceptions.

One of those exceptions for the Department of Energy (DOE) is for personal information when it is required for an authorized health study. The conditions of such a release include the assurance that researchers understand that they are under the same obligation to safeguard personal information as DOE employees.

The problem: Many DOE record holders, Institutional Review Boards (IRBs), and certainly researchers are unaware of the existence of this provision of the law, and Privacy Act Officers are rarely a part of the equation.

The solution at Hanford: We are working to create a process by which legal requirements are made known to researchers and their agreement to comply with them is assured prior to access to personal information.

Speaker: Chris Kuczynski, Equal Employment Opportunity Commission, Washington, DC

Topic: *Genetic Privacy under the ADA.*
The Americans with Disabilities Act (ADA) of 1990 limits the circumstances under which employers may acquire, use, and disclose medical information about employees and applicants for employment.

> *"The ADA prohibits employers from asking disability-related questions."*

The ADA prohibits employers from asking disability-related questions or requiring medical examinations before a conditional offer of employment is made. After a job offer is made but before employment begins, an employer may ask disability-related questions and require medical examinations, including questions and examinations that reveal genetic information, as long as the employer does so for all applicants in the same job category.

If an employer withdraws a job offer from an applicant with a disability based on the answers to disability-related questions or the result of medical examinations, the employer must be able to show that this decision was job-related and consistent with business necessity.

Once employment begins, an employer may only ask disability-related questions and may only require medical examinations that are job-related and consistent with business necessity. All medical information about an applicant or employee must be kept confidential, with limited exceptions.

This presentation considered how these principles apply to the acquisition, use, and maintenance of genetic information, particularly information that indicates only an increased risk of acquiring a particular condition. Also discussed were the possible implications of Bragdon v. Abbott for individuals seeking ADA protection on the basis of genetic information. This 1998

Supreme Court decision held that the plaintiff's asymptomatic HIV-positive status constituted a disability within the meaning of the ADA.

SESSION 5
Communicating risk

Speaker: Maria Pavlova, Office of Occupational Medicine and Medical Surveillance, U.S. Department of Energy, Germantown, Maryland.

Topic: *Effective Workplace Communication: Whose Responsibility?* Employers are required to communicate about the risks associated with workplace hazards under various laws. However, we find from research and from our own experiences that a legalistic, one-way approach to communication is less likely to help us meet our goals than communication that is truly two-way.

Two-way communication is conducted on common ground where individuals coming from many perspectives listen to each other's ideas and concerns not necessarily with agreement but with respect.

Two-way communication both requires trust and builds trust. Although managers must usually take the first steps in creating an atmosphere supportive of consensus-building and collaboration, maintaining that atmosphere becomes everyone's responsibility. Risk communication principles and practices also apply in workplace medical surveillance and occupational health research.

At one level, informed consent can be viewed as a special case of risk communication. Worker's rights and welfare will be best protected and the research outcomes will be most useful if occupational studies begin with structured efforts to build a collaborative and cooperative relationship among all participants.

Speaker: Carol Taylor, Health Care Ethicist, Center for Clinical Bioethics, Georgetown University.

Topic: *Individual and Corporate Integrity: Why We Need Organizational Ethics.* A dictionary defines integrity as: (1) soundness of and adherence to moral principle and character; uprightness and honesty. (2) the state of being whole, entire, or undiminished. (3) a sound, unimpaired, or perfect condition. Moral integrity is that condition or state in which moral activity (valuing, choosing, acting) is intimately linked to a particular conception of what it means to live a good life.

This session explored personal and corporate integrity as they relate to organizational ethics. Participants were led in an exploration of how organizational integrity is developed, monitored, and rewarded. The consequences of honoring and dishonoring integrity were also examined.

A corporation is said to have moral integrity if there is a good fit between the corporation's everyday decision making and its stated mission, purpose, and core values.

A corporation develops integrity by 1. dedicating time and space to reflect on, articulate and own a particular conception of what is considered the Good, and what is considered the "Good" Corporation.

2. practicing valuing, choosing, and acting according to the corporation's conception of what fidelity to the good/good life demands. It is especially important to develop a habitual disposition to value, choose and act in accordance with one's moral code.

3. reflecting on the consequences of honoring and dishonoring integrity.

A corporation is said to have moral integrity if there is a good fit between the corporation's everyday decision making and its stated mission, purpose and core values.

—Carol Taylor

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The partnership has created communications methods and materials that are easily understood.

—Sherry Davis-Cross and Knut Ringen

4. developing a culture and structures that support ethical behavior and acting with integrity (there should be incentives, not disincentives for doing the right thing for the right reasons).

The role of an organization’s ethics advisor is to ensure a good fit between a system’s stated mission, the organization’s core values, decision making, and the responsible behavior of administrators and employees.

Speakers: Sherry Davis-Cross, Battelle Pacific Northwest National Laboratory Richland, Washington, and **Knut Ringen**, The Center to Protect Worker’s Rights, Washington, DC.

Topic: *Researcher and IRB partnership as a model for good communication.*

Working together, we have succeeded in addressing and resolving conflicting concepts. The effort was effective because both of us are concerned with the protection and welfare of workers.

This goal overcame possible program issues that are commonly experienced among agencies that fund research, the sites where research is conducted, the Institutional Review Boards, the researchers who conduct the research, and in particular the workers themselves. The partnership has created communications methods and materials that are easily understood, comprehensive, and available as models for anyone who is interested.Δ

DOE Database update

Former worker projects, questionnaire, epidemiology studies added

Several significant events occurred during the fiscal year 1999 update to the DOE Human Subjects Research Database (HSRD). A new state-of-the-art Web-based questionnaire—designed for efficiency and ease of use while maintaining extensive data checking algorithms—was used for the first time. Developed using new Internet tools and technologies, the questionnaire is faster, better, and cheaper than its FoxPro predecessor. The new Web questionnaire was very well received, and a number of contributors praised the system for its ease of use and time-saving performance.

In addition, for the first time, information from the DOE Former Worker Projects and NIOSH epidemiology studies has been submitted to the database. This encouraging news has resulted from increased collaboration and cooperation between organizations conducting studies that involve human subjects at DOE facilities.

Finally, a new employee, Ethel Jacob, has joined the HSRD database team, bringing new energy, ideas, and assistance.

The HSRD provides information on research projects that involve human subjects and that are funded by DOE, conducted at DOE facilities, or performed by DOE personnel.The database is at http://www.eml.doe.gov.hsrd/. It is updated every year. For information, contact Richard Larsen, DOE Environmental Measurements Laboratory, larsenr@eml.doe.gov.Δ

Exxon's commitment

Controlling health & safety risks

By Myron C. Harrison, M.D., Director, U.S. Medicine & Occupational Health Services, Exxon Co.

Recognizing and controlling health and safety risks is a substantial part of Exxon's responsibility. Recognition of health risks depends, in part, upon research on groups of employees who have similar exposures to potentially hazardous materials.

The company's health policies (available at www.exxon.com) are designed to assist and protect its employees. Communicating information about health issues is one of the primary elements of the policies. This requires that we communicate knowledge about health risks gained from Exxon health programs and related studies. It also requires that information about employees obtained through implementation of these programs be kept confidential.

Myron Harrison

Exxon ensures implementation of the policies through its Operations Integrity Management System (OIMS), which defines objectives, maintains accountability and documentation, measures results, and develops feedback mechanisms. Line management has the ultimate responsibility for fulfilling expectations created in OIMS. Staff support functions provide professional services and expertise.

One of these is Exxon's Medicine and Occupational Health Department (MOHD), an organization of approximately 360 physicians, nurses, industrial hygienists, and administrators. The health research arm of MOHD is Exxon Biomedical Sciences, Inc. (EBSI), which maintains the Exxon Cohort Mortality Study.

Standardized Mortality Ratios (SMRs) are calculated by comparing actual numbers of deaths by cause to expected numbers of deaths based upon national statistics. In the most recent update of the Mortality Study, the overall SMR was 58%.

This means that the overall age adjusted death rate for this group was 42% less than national norms. While the overall rate is reassuring (and not atypical of employed, upper socioeconomic cohorts), the analysis looks in greater detail at specific groups of workers and specific sites by disease category.

A second, more detailed, analysis found elevated rates of chronic lymphocytic leukemia (CLL) at Exxon's Baton Rouge Refinery. There was a small excess of CLL for the overall U.S. cohort (though not statistically significant), but a statistically significant threefold excess at the Baton Rouge site (10 observed cases compared to three expected).

One of the first steps was to communicate the results to Exxon management and employees in a series of presentations at several locations and articles in company papers. External communication was accomplished with publication in a peer-reviewed journal.

—Continued on page 17

"MOHD is an organization of approximately 360 physicians, nurses, industrial hygienists, and administrative personnel who deliver medical and industrial hygiene services to Exxon employees worldwide."

The Working Group

From small beginnings

Only a small gathering of IRB administrators and chairs attended the first meeting of the Department of Energy's (DOE's) Human Subjects Working Group (HSWG).

But that 1988 meeting was to be the beginning of what would become a strongly influential group comprised of DOE field and headquarters officials, Institutional Review Board (IRB) members, program and project managers, other government agency officials (NIH, NIOSH), university and hospital staff, various experts, and former DOE workers.

When Dr. Susan L. Rose created the HSWG for what is now DOE's Office of Science, her goal was an umbrella group providing educational and networking opportunities for the DOE human subjects community. Thus the HSWG formalized DOE's commitment to protecting human subjects in research studies.

The people she gathered represent not just the range of constituencies involved with human subjects, they also include a range of experience, wisdom, and concerns. Several, like IRB administrators Darcy Mallon and Chris Byrne, are involved with clinical research. Others, like Sherry Davis-Cross at Battelle Pacific Northwest, work almost entirely with laboratory research and workplace studies.

Also included are people with very unusual skills. DOE's Michael Mazaleski, a member of the U.S. Army's IRB, is the group's resident guru for classified programs. There are newer IRB administrators, like Linda Sundberg, Terry Reser, and Bree Klotter, who are doing an excellent job in very controversial areas, and Martha DeMarre, of the Nevada Test Site, who is beginning an IRB from scratch.

There are also those who have been at this for a very long time, like Shirley Fry, John Jankovic, Alan Rither, and Don Grube, who have been doing this successfully for many years.

John Campbell, Glenn Bell, and Reed Durham bring to the group the unique perspective of having been subjects of workplace studies.

Special views are added by Bill Nebo, senior pastor at a Livermore, California, church. Mikki Dawn and

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HSWG's troubleshooter

Charles Pietri

Charles Pietri, an original member of the Human Subjects Working Group in the mid-1980s, remains instrumental in shaping and advising the DOE workgroup in particular and providing guidance on DOE policies in general. His special contributions include utilizing the diversity of the group's membership and keeping attention focused on its purpose and goals.

Pietri's involvement began when he was science administrator and manager for institutional programs at DOE's Chicago Operations Office. Thus he brings to this task the benefit of his DOE experience, but he also brings an invaluable understanding from his prior experience as a researcher.

For many years, Susan Rose has relied on Pietri's humor, insight, experience, and wisdom. When problems arise, his unique abilities are often required. Pietri is counted on both as a troubleshooter and source of advice, and his involvement

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New DOE policy

Protection of Human Subjects

Department of Energy (DOE) directives include policies, orders, notices, manuals, and guides which are intended to direct, guide, inform, and instruct employees in the performance of their jobs and enable them to work effectively within the Department and with agencies, contractors, and the public. DOE orders may include a contractors requirements document, which stipulates the conditions under which a DOE contractor is expected to perform.

On August 29, 1990, the first order on the Protection of Human Subjects, DOE Order 1300.3, was issued. It provided minimal guidance and direction to implement provisions of the *Code of Federal Regulations* (CFR) for the Protection of Human Subjects, 10 CFR Part 745, which set out federal requirements for DOE for the protection of human subjects involved in research activities.

In the following years, especially with the advent of increased research involving human subjects including the human genome program and worker studies projects, it became apparent that the existing order lacked sufficient detail and guidance to be effective as originally intended. Early in 1999, at the suggestion of the DOE Office of Management and Administration, the Office of Science initiated a task to update the existing order.

A team lead by Dr. Susan Rose, Program Manager for the Human Subjects Research Program (SC-72), has recently completed revision of this order. The team consisted of Sally Bennett, technical writer, Enterprise Advisory Services, Inc.; Vicki Prouty, attorney, Chicago Operations Office; and Charles Pietri, consultant, HITECH Consultants.

A policy document, DOE P-440.X, *Policy on the Protection of Human Subjects*, was created separately from the new order to ensure a clearer definition of the DOE policy for the protection of human subjects in research activities.

The new order, DOE O-440.X, Protection of Human Subjects, is structured to provide an improved statement of requirements for the protection of human subjects, expanded definitions relevant to human subjects research protections, enhanced responsibilities for DOE program and field management, and a clear set of requirements for the contractor.

Both documents were processed through the DOE Management Directives System, which encouraged all DOE departmental elements to comment on the drafts. Numerous comments were received, many with constructive suggestions for improvement or clarification of the order and policy. All comments were addressed and issues resolved. In addition, helpful comments and suggestions were received from members of the DOE Human Subjects Working Group as well as other interested parties.

The draft policy and the order are being prepared for transmittal to the Office of Management and Administration for assignment of document numbers and publication. This newsletter will announce its publication.Δ

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A policy document was created separately from the new order to ensure a clearer definition of the DOE policy for the protection of human subjects in research activities.

ORI is reassigned & misconduct defined

Scientific Research

The Office of Research Integrity (ORI) will no longer conduct investigations of scientific misconduct and, along with that change, misconduct itself is being redefined.

The change at ORI, implemented by the Department of Health and Human Services (HHS), means that it will now have only an oversight and recommendation role, says Chris Pascal, ORI's acting director.

> *"The new definition of misconduct narrows it to three acts: fabrication, falsification, and plagiarism.*

The new definition of misconduct, suggested by the White House's Office of Science and Technology Policy (OSTP), narrows misconduct to three acts: fabrication, falsification, and plagiarism.

HHS Secretary Donna Shalala said her department will adopt the newly proposed definition, which was published October 14 in the *Federal Register.*

Speaking for the Federation of American Societies for Experimental Biology, Howard Schachman, a University of California, Berkeley biochemist, said he is pleased with both developments: "I'm ecstatic about how this has come out."

Since 1992 ORI has investigated misconduct by HHS-funded researchers and imposed sanctions. But four years ago a Congressionally appointed commission recommended that ORI be stripped of those tasks.

In its new role, ORI and HHS will be dependent primarily on a research institution's own investigation, which will be reviewed by ORI. The office will make recommendations for sanctions but will no longer have the authority to impose them.

In addition, ORI is launching a pilot project to assist institutions to do their own investigations. This is similar to the policy at the National Science Foundation (NSF), where investigations are conducted by the Inspector General, who makes recommendations for sanctions to the NSF.

The proposed new definition for scientific misconduct would eliminate part of the definition that has been used by both HHS and NSF. The definition currently encompasses fabrication, falsification, plagiarism, and "other serious deviations" from accepted practice. The last clause has often been criticized as too vague. To replace it, the White House suggests: "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results."

The definition also spells out what it means by fabrication, falsification, and plagiarism. For example, fabrication is "making up results and recording or reporting them." Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit, including those obtained through confidential review of others' research proposals and manuscripts.Δ

Web sites

Report of the Workshop on Population-Based Samples for the NIGMS Human Genetic Cell Repository. *http://www.nih.gov/nigms/news/reports/cellrepos.html*

The National Bioethics Advisory Commission's (NBAC's) final report "Research Involving Human Biological Materials: Ethical Issues and Policy Guidance," August 1999. It is under reports at *http://bioethics.gov/*

Human Genetic Cell Repository, sponsored by the National Institute of General Medical Sciences (NIGMS). *http://locus.umdnj.edu/nigms/*

Standards for Privacy of Individually Identifiable Health Information, Notice of Proposed Rule Making (NPRM) is available through the internet at the locations below. Published November 3, 1999. Comment period ended January 3, 2000.
http://aspe.hhs.gov/admnsimp/
http://www.hhs.gov/hottopics/healthinfo/index.html
http://erm.aspe.hhs.gov/ora_web/plsql/erm_rule.library

University of Houston Health Law News: Quarterly publication of the University of Houston, Health Law & Policy Institute. For subscriptions, email: healthlaw@uh.edu.
http://*www.law.uh.edu/healthlawnews/homepage.html*

Each issue of Health Law News has a special section on a health law subject.
Medical Privacy was covered in the March 1999, Vol. XII, No. 3 issue of the newsletter
http://www.law.uh.edu/healthlawnews/03-1999.html

Exxon's commitment

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The 10 cases all occurred among employees hired during the 1940s. It was important to determine whether the excess of CLL deaths was related to work exposures still present and whether it was a random event. Collaborating with Dr. Vivian Chen, director of the Louisiana Tumor Registry (LTR), Exxon began a study to look for more current CLL cases.

EBSI and LTR researchers prepared a detail protocol, which was submitted to the Louisiana State University Medical Center's IRB for approval.

The protocols (and, eventually, the data and study results) were reviewed by an external scientific advisory board. Agreements were written on use of data and review of publications. Protection of participant privacy was assured.

The study has been completed and the results communicated to management and employees within Exxon. A report of the study, coauthored by EBSI and LTR scientists, has been submitted for publication.Δ

> *"It was important to determine whether the excess of CLL deaths was related to work exposures still present and whether it was a random event.*

Charles Pietri, troubleshooter

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and contributions may be felt in every product, meeting, and action involving human subject protections at DOE. He deserves special thanks and acknowledgment from us all for providing vital and irreplaceable advice and support to the program.Δ

From small beginnings

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Becky Hawkins of Oak Ridge add energy, humor, and administrative skills.

Debbie Marcantonio, Bill Bunn, Dean Decker, and Thrish St. Clair, representing DOE-wide operations offices, bring to the group oversight and responsibility for DOE labs.

Bringing computer expertise to the job are Richard Larsen and Camille Marinetti, who are responsible for the annual DOE human subjects program database (see page 12).

To strengthen and enrich the group, it has adopted academic IRB admistrators Paula Knudson, Marianne Elliott, Steven Peckman, Mary Rutz, and NIOSH members.

> *"It is this diversity of interest, perspective, skills, and experience that makes HSWG effective in protecting human subjects.*

It is this diversity of interest, perspective, skills, and experience that makes HSWG effective in protecting human subjects. When they gather for meetings, which happens formally once or twice a year in conjunction with the PRIM&R and ARENA meetings or the Interagency Conferences, they combine their efforts to solve problems in ways that with less diversity would be far less effective. During the rest of the year, their access to each other provides a network of resources that is a powerful tool for solving specific problems.

The group has increased its effectiveness by publishing the DOE *Human Subjects Research Handbook*, which provides a distilled version of all the members' knowledge about the field. It is a sourcebook both for people already involved in human subjects protection and those just setting up programs.

Members also share their combined skills by participating in the DOE Human Subjects Performance Reviews conducted periodically by Dr. Rose and a panel of national experts. The combination of all these efforts has helped ensure the integrity of research throughout the scope of DOE's programs.

You can find more details about the working group members and how to contact them at: www.er.doe.gov/production/ober/humsubj/list4.htmlΔ

Food for the soul

Reflections on the working group from new IRB administrator Terry Reser

The annual Public Responsibility In Medicine & Research (PRIM&R) and Applied Research Ethics National Association (ARENA) conference provides a cornucopia of food for the soul and a chance to hang around the coffee pot with the movers and shakers of the IRB world as well as our merely overburdened fellow folk.

For me, the real highlight of these annual gatherings is the DOE Human Subjects Working Group (HSWG) meeting, which coincides with PRIM&R to minimize travel costs and maximize the pool of experts on hand.

In Boston this year, the Director of the Office for Protection from Research Risks (OPRR), Gary Ellis, stated that his organization simply could not function without PRIM&R. As a relatively new IRB Administrator, I am similarly dependent on the HSWG and

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Protecting Human Subjects

This bulletin is designed to facilitate communication among those involved in human subjects research and to inform persons interested in human subjects research activities.

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This newsletter is available at no cost to anyone interested or involved in human subjects research at DOE. Please send name and complete address (printed or typed) to the address below. Please indicate whether information is to (1) add new subscriber, (2) change name/address, or (3) remove name from mailing list. Enclose a business card, if possible.

Send suggestions, contributions, and subscription information to —

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Meetings

May 3–5, 2000
Protection of Human Subjects: The Myth of Privacy and Confidentiality Explored.
Tampa, Florida
Contact: Darlene Marie Ross, Office for Protection from Research Risks, National Institutes of Health.
Telephone: (301) 435-5648. Fax: (301) 402-0527. Email: dr20a@nih.gov.
http://grants.nih.gov/grants/oprr/97humanworkshop.htm

May 12, 2000
PRIM&R/AAMC Regional Workshops on Effective IRBs
San Diego Marriott Mission Valley • San Diego, California.
Sponsor: The Association of American Medical Colleges and Public Responsibility in Medicine and Research (PRIM&R).
The workshop is designed to improve the effectiveness of Institutional Review Boards by instructing administrators, IRB members, clinical investigators, and research staff in the fundamentals of human subjects protection and IRB functioning.

Contact: www.aamc.org/meetings/specmtgs/irb00/overview.htm

June 2000
Protection of Human Subjects: The Myth of Privacy and Confidentiality Explored.
Rush Presbyterian-St. Luke's Medical Center • Chicago, Illinois
Contact: Darlene Marie Ross (see above).

August 2000
Protection of Human Subjects: The Myth of Privacy and Confidentiality Explored.
Portland, Oregon
Contact: Darlene Marie Ross (see above).

Notes from Sandia's new IRB chief

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PRIM&R and ARENA provide thought-provoking, well-rounded presentations and intriguing contacts. Both are valuable tools that make my job easier, and I always come away from their conferences with useful information. However, those gems are usually buried in volumes of pages or presentations that reflect an overwhelmingly clinical orientation far removed from the day-to-day reality at my site. It's a bit like a going-out-of-business sale: there are treasures to be had, but it usually takes a lot of sorting through to find something that fits.

In contrast, the HSWG is essential — it provides relevant, reliable, timely information and critical discussions of issues that directly affect my board. It also allows me to network with kindred DOE'ers who share similar sites, situations, and problems, and whom I'm most likely to call with questions or concerns.

So, as I reflect on this year's conference (a recently acquired coping strategy to delay having to tackle the stack of work that piled up while I was gone), I'm grateful to Dr. Susan Rose (and Kim Laing, Mikki Dawn, and others who deal with the devilish details) for the foresight, fortitude, and patience it takes to plan and pull off these meetings. You do nice work!Δ

Terry J. Reser, Sandia National Laboratory

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